Cutting Through the Cholesterol Confusion
“...available evidence shows no appreciable relationship between consumption of dietary cholesterol and serum cholesterol.... Cholesterol is not a nutrient of concern for overconsumption.”
Americans Less Worried about Fat

Gallup Poll, July 8-12, 2015
1,009 adults

*Americans' Dietary Habits of Eating Fat*

Thinking about the food you eat, for each of the following please say if it is something you actively try to include in your diet, something you actively try to avoid, or something you don’t think about either way.

How about fat?

<table>
<thead>
<tr>
<th>Year</th>
<th>% Include</th>
<th>% Avoid</th>
<th>% Don’t think about</th>
</tr>
</thead>
<tbody>
<tr>
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<td>62</td>
<td>21</td>
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<td>'06</td>
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<td>'07</td>
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<td>'08</td>
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<td>'14</td>
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</tr>
<tr>
<td>'15</td>
<td>47</td>
<td>22</td>
<td>21</td>
</tr>
</tbody>
</table>

GALLUP
Americans Less Worried about Salt

Gallup Poll, July 8-12, 2015
1,009 adults

Gallup's recent survey found that a smaller percentage of Americans are actively trying to avoid salt in their diet compared to previous years. The graph illustrates the trends from 2002 to 2015, showing a decrease in the percentage of adults who actively avoid salt, while the percentage of those who include it in their diet remains relatively stable. The data suggests a shift in dietary habits over time.
Understanding Cholesterol
Chole = bile
Cholesterol is a key part of cell membranes.
Cholesterol is a raw material for building hormones.
Cholesterol

4 rings in 6,6,6,5 pattern

8-carbon side chain
Cholesterol
Cholesterol $\rightarrow$ Testosterone
Cholesterol

Testosterone

Estradiol
Cholesterol Makes Vitamin D
7-Dehydrocholesterol $\rightarrow$ Vitamin D$_3$
Cholesterol contributes to cardiovascular disease.
Where Does Cholesterol Come From?

Produced in all animal cells, especially liver cells.

About 1 gram per day.
Saturated Fat Stimulates Cholesterol Production

1% ↑ saturated fat → 2% ↑ LDL

Cholesterol from Food Products

There is no requirement for dietary cholesterol.

40-60% of ingested cholesterol is absorbed (proximal jejunum).

Chylomicrons escort cholesterol into the circulatory system.
Does cholesterol in foods increase cholesterol levels in the blood?
Early Studies

Ancel Keys, University of Minnesota
Mark Hegsted, Harvard University

Dietary cholesterol increases blood cholesterol.

Curvilinear effect: Greatest effect at lower intakes.
Early Studies

At common intake levels, the relationship is linear.
Linear Effect at Lower Intakes

$X \times 0.0974 = Y$

$X \times 0.1 = Y$

$X = \text{dietary cholesterol change per 1000 kcal}$

$Y = \text{change in serum cholesterol in mg/dL}$

Example: 1 egg (~200 mg of cholesterol)
Assume a 2,000-calorie diet

100 mg cholesterol × 0.1 = 10 mg/dL

Harvard Study: Eggs and Cholesterol

17 ovo-lacto-vegetarian students, previously averaging 3 eggs per week.

Adding 1 extra-large egg per day for 3 weeks:

Total: +11.6 mg/dL
LDL: +6.8 mg/dL (no effect on particle size)
HDL: -2.5 mg/dL
TG: +2.9 mg/dL

Eggs vs Egg Substitute: Crossover Trial

Meta-Analyses

Meta-Analysis: 224 studies (Howell 1997)

100 mg/d ↓ in dietary cholesterol  ↓ 2.2 mg/dL (57 µmol/L) in total cholesterol

Meta-analysis: 395 Diet Experiments (Clarke 1997)

↓ Dietary cholesterol by 200 mg

TC ↓ 5.0 mg/dL (0.13 mmol/l)

LDL ↓ 3.9 mg/dL (0.10 mmol/l)

Meta-analysis: Cholesterol from Eggs (Weggemans 2001)

17 studies

100 mg dietary cholesterol

TC ↑2.2 mg/dL
(0.056 mmol/L)

TC:HDL ratio ↑ 0.02 units

Meta-Analysis: 18 Intervention Trials (Berger 2015)

Increasing dietary cholesterol (combined result):

Total Cholesterol ↑ 11.2 mg/dL


Funded by USDA agreement 1950-51000-073 and the American Egg Board, Egg Nutrition Center.
Institute of Medicine

↑ Dietary cholesterol 100 mg/d

↑ LDL ~ 2 mg/dL (0.05 mmol/L)

Conclusions

• Dietary cholesterol increases blood cholesterol.

• The increase is greatest at lower levels of baseline cholesterol intake.

• The increase is significant from a public health standpoint.

• Compensatory mechanisms do not prevent cholesterol elevations.
“…available evidence shows no appreciable relationship between consumption of dietary cholesterol and serum cholesterol, consistent with the conclusions of the AHA/ACC report.”
AHA/ACC Report

The AHA/ACC did not state that dietary cholesterol has “no appreciable effect” on serum cholesterol.

Limited to evidence published 1998-2009, omitting most meta-analyses.

Called for additional research, particularly on lower levels of cholesterol and saturated fat intake.

“Nevertheless, when ordering an omelet, why not order an egg white omelet with plenty of vegetables, lean meat, and spices rather than one with 600 mg cholesterol?”

Read the Fine Print
Describing a study by Schonfeld (1982):

20 men

Compared 3 eggs (750 mg) and 6 eggs (1500 mg)

Varied the polyunsaturated to saturated fat ratios.

P:S ratio of 0.25-0.4:
3 eggs increased LDL by 16 mg/dL
6 eggs increased LDL by 25 mg/dL

P:S ratio of 0.8:
Only 6 eggs increased LDL, by 17 mg/dL
(Omitted: 3 eggs increased LDL by 9 mg/dL)

P:S of 2.5:
Neither amount of cholesterol intake produced significant changes in LDL.
(Omitted: 3 eggs increased LDL by 6 mg/dL, and 6 eggs increased cholesterol by 10 mg/dL)
**Schonfeld 1982**

**FIGURE 1** Dietary cholesterol-induced changes in fasting plasma LDL cholesterol concentrations (LDL-C). Results are means±1 SEM, expressed as increments or decrements compared to the Basal1 diet. (See Table II for numbers per group.) **P < 0.01, *P < 0.02, by paired two-tailed t test.**

Does It Matter?
Cholesterol Travels with Saturated Fat

2 eggs:

362 mg cholesterol

+ 3.1 g saturated fat (19% of calories)
Sources of Cholesterol in the U.S. Diet

# Animal Products

<table>
<thead>
<tr>
<th>Food</th>
<th>Cholesterol</th>
<th>Saturated Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Large eggs</td>
<td>362 mg</td>
<td>3.1 g (19%)</td>
</tr>
<tr>
<td>Chicken with skin (100 g)</td>
<td>88 mg</td>
<td>3.8 g (14%)</td>
</tr>
<tr>
<td>without skin (100 g)</td>
<td>89 mg</td>
<td>2.0 g (10%)</td>
</tr>
<tr>
<td>Roast beef, lean only (100 g)</td>
<td>83 mg</td>
<td>3.4 g (17%)</td>
</tr>
<tr>
<td>Chinook salmon (100 g)</td>
<td>85 mg</td>
<td>3.2 g (13%)</td>
</tr>
<tr>
<td>Cheddar cheese (2 oz)</td>
<td>58 mg</td>
<td>11.0 g (43%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Plant Products</th>
<th>Cholesterol</th>
<th>Saturated Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black beans (100 g)</td>
<td>0</td>
<td>0.1 g (1%)</td>
</tr>
<tr>
<td>Brown rice (100 g)</td>
<td>0</td>
<td>0.2 g (1%)</td>
</tr>
<tr>
<td>Broccoli (100 g)</td>
<td>0</td>
<td>0.1 g (3%)</td>
</tr>
<tr>
<td>Sweet potato (100 g)</td>
<td>0</td>
<td>0.04 g (0.5%)</td>
</tr>
</tbody>
</table>

What About Eggs?
Eggs and Diabetes: Meta-Analyses

Li, 2013: Increased risk of diabetes.

Shin, 2013: Frequent egg consumption: 42% increased risk of developing diabetes.


Eggs and CVD

Li, 2013 meta-analysis: Increased risk of cardiovascular disease.

Shin, 2013 meta-analysis: Increased CVD risk only in people with diabetes. One egg per day was associated with a 69% higher risk of cardiovascular complications.


What is the solution?
Statins

Highly effective for lowering cholesterol.
Statins

• Muscle pain
• Liver damage
• Diabetes risk
• Increase blood glucose
• Weight gain
Statins and Glycemic Control

Weill Cornell Medical College

Meta-analysis: 9 studies, 9,696 participants

3.6-year follow-up

A1c ↑ 0.12 points.

Statins

- Muscle pain
- Liver damage
- Diabetes risk
- Increased blood glucose
- Weight gain
- Memory problems
Effects of Plant-Based Diets in Hyperlipidemic Individuals: Randomized Controlled Trials

- Gardner 2005
- Appel 2005 - protein
- Appel 2005 - monounsaturated
- Kestin 1989
- Ornish 1990
- Ornish 1998‡
- Jenkins 2003
- Jenkins 2003
- Jenkins 2005
- Jenkins 2006

Absolute Mean Cholesterol Difference (mg/dL) (Intervention Versus Control Group)

‡5 year follow-up or Ornish 1990

Effects of Plant-Based Diets
Randomized Controlled Trials
Normolipidemic Participants

Trial (Author/Year)

Cooper 1982
Hunt 1997
Jenkins 1997
Barnard 2000
Barnard 2006

Vegan

Vegetarian

Absolute Mean Cholesterol Difference (mg/dL)
(Intervention Versus Control Group)

TC
LDL-C
HDL-C
Special Cholesterol-Lowering Foods

Soluble fiber (oats, barley, eggplant, okra, psyllium): 20 grams

Soy protein (soy milk and soy meat analogues): 40 grams

Whole almonds: 28 grams

Sterol/stanol-enriched margarine: 2 grams

Listed quantities are for a 2,000-calorie diet

Special Cholesterol-Lowering Foods

In 4 weeks:

LDL ("bad") cholesterol -29%

For comparison, cholesterol-lowering drugs -31%

Side Effects of a Plant-Based Diet
### Plant-Based Diets Reduce Body Weight

<table>
<thead>
<tr>
<th>Study name</th>
<th>Subgroup within study</th>
<th>Mean</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferdowsian 2010 (26)</td>
<td>Vegan</td>
<td>-5.1</td>
<td>-6.3</td>
<td>-3.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Barnard 2009 (24)</td>
<td>Vegan</td>
<td>-3.7</td>
<td>-5.5</td>
<td>-1.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Turner-McGrievy 2007 (22)</td>
<td>Vegan</td>
<td>-3.6</td>
<td>-6.0</td>
<td>-1.2</td>
<td>0.003</td>
</tr>
<tr>
<td>Dansinger 2005 (21)</td>
<td>Vegetarian</td>
<td>-3.3</td>
<td>-5.6</td>
<td>-1.0</td>
<td>0.004</td>
</tr>
<tr>
<td>Mishra 2013b (27)</td>
<td>Vegan</td>
<td>-3.0</td>
<td>-3.8</td>
<td>-2.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Kjeldsen-Kragh 1991 (14)</td>
<td>Vegetarian</td>
<td>-2.9</td>
<td>-4.2</td>
<td>-1.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mishra 2013a (27)</td>
<td>Vegan</td>
<td>-2.9</td>
<td>-3.6</td>
<td>-2.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gardner 2007 (23)</td>
<td>Vegetarian</td>
<td>-2.6</td>
<td>-3.8</td>
<td>-1.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Nenonen 1998 (17)</td>
<td>Vegan</td>
<td>-1.8</td>
<td>-2.8</td>
<td>-0.8</td>
<td>0.0002</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>-3.1</td>
<td>-3.7</td>
<td>-2.5</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Plant-Based Diets Reduce HbA1c

<table>
<thead>
<tr>
<th>Study name</th>
<th>Subgroup within study</th>
<th>Difference in means</th>
<th>Difference in means and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferdowsian et al., 2010</td>
<td>low fat vegan</td>
<td>-0.700</td>
<td>[ -1.06, -0.34 ]</td>
</tr>
<tr>
<td>Mishra et al., 2013</td>
<td>low fat vegan</td>
<td>-0.700</td>
<td>[ -1.06, -0.34 ]</td>
</tr>
<tr>
<td>Barnard et al., 2009</td>
<td>low fat vegan</td>
<td>-0.410</td>
<td>[ -0.67, -0.15 ]</td>
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<tr>
<td>Nicholson et al., 1999</td>
<td>low fat vegan</td>
<td>-0.400</td>
<td>[ -0.66, -0.14 ]</td>
</tr>
<tr>
<td>Kahleova et al., 2011</td>
<td>lacto vegetarian</td>
<td>-0.387</td>
<td>[ -0.65, -0.12 ]</td>
</tr>
</tbody>
</table>

Combined effect = 0.39

Plant-based diets also reduce blood pressure.

BP, systolic observational studies

Plant-based diets also reduce blood pressure.

Systolic and diastolic BP in clinical trials

Saturated Fat
“Butter is back, and when you’re looking for a few chunks of pork for a stew, you can resume searching for the best pieces — the ones with the most fat.”

“Saturated fat does not cause heart disease—or so concluded a big study published in the journal Annals of Internal Medicine.”

Nina Teicholz. The Questionable Link Between Saturated Fat and Heart Disease. WSJ, May 6, 2014
Saturated Fat and Coronary Disease
